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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,291	02/05/2007	Tsvee Lapidot	30694/42021	6831

4743 7590 11/06/2009

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
11/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,291	LAPIDOT ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 26-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 24 August 2009.

Claim Status

Claims 1-40 are pending. However, claims 1-16 and 26-40 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR § 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 17-25 are amended. Claims 17-25 are under current examination.

Priority

This application claims benefit as a 371 of PCT/IL04/01018 (filed 11/08/2004). This application also claims benefit from foreign application ISRAEL 158868 (filed 11/13/2003). The instant application has been granted the benefit date, 13 November 2003, from the foreign application, ISRAEL 158868.

RESPONSE TO ARGUMENTS

Claim Objections

The objection to claims 24-25 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn.

35 USC § 112, 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 17-22 and 24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to the applicant's claim amendments.

However, claims 23 and 25 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record and the comments below.

Claims 23 and 25 recite "at least about." MPEP2173.05(b) indicates the court held that claims reciting "at least about" were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the term "about." *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991). Therefore, claims 23 and 25 should be amended to clarify the recited ranges.

The applicant has argued that the rejection based upon the use of the phrase "at last about," is improper because the cited referenced do not teach or suggest the subject matter of amended claims 23 and 25 (Remarks, page 9 2nd parag.). Contrary to

the applicant's assertion, these claims 23 and 25 are rejected over art (Sawada et al and Lapidot et al.) Therefore, the examiner finds the applicant's argument unpersuasive.

Accordingly, the examiner maintains the rejection of claims 23 and 25 under 35 USC 112, 2nd.

35 USC § 101

The rejection of claims 17-25 under 35 USC §101 because the claimed invention is directed to non-statutory subject matter is withdrawn in response to the applicant's claim amendments. The applicant has amended the instant claims to recite "isolated population." This language is sufficient to overcome the non-statutory rejection.

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Sawada

Claims 17-19 and 24-25 remain rejected under 35 U.S.C. 102(b) as being anticipated by Sawada et al (J. Exp. Med., May 4, 1998; 187(9): 1439-1449) for the reasons of record and the comments below.

The applicant's arguments have been fully considered but are unpersuasive.

The applicant argues that a transgenic mouse comprising stem cells having a transgene encoding CXCR4 is not an isolated population of stem cells having a transgene encoding CXCR4 (remarks, page 11, 1st parag.). While this may be true, Sawada teaches isolated peripheral blood from the transgenic mice (i.e., page 1443, col.2, Discussion). Since Sawada was in the possession of peripheral blood from a transgenic mouse comprising stem cells having a transgene encoding CXCR4, and peripheral blood is know to have some hematopoietic stem cells, the examiner concludes that Sawada anticipates an isolated population of stem cells having a transgene encoding CXCR4, wherein the isolated population comprises a high amount of immature primitive progenitor cells. The examiner points out that the specification does not provide a limiting definition for the phrase "a high amount of immature primitive progenitor cells." Therefore, the applicant's arguments are unpersuasive

Therefore, the examiner hereby maintains the rejection of claims 17-19 and 24-25 under 35 U.S.C. 102(b) as being anticipated by Sawada et al.

The examiner reiterates the pending rejection:

Claims 17-19 and 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Sawada et al (J. Exp. Med., May 4, 1998; 187(9): 1439-1449).

Claim 17 is directed to an isolated population of stem cells comprising a transgene encoding CXCR4 and exhibiting improved CXCR4 signaling capability in response to low and/or high concentration of SDF-1, wherein the isolated population comprises a high amount of immature primitive progenitors. Sawada et al. teach a

transgenic mouse comprising a human CXCR4 gene (page 1440, Materials). The transgenic mouse comprises a cell population comprising stem cells having the CXCR4 gene. Sawada was in the possession of peripheral blood from a transgenic mouse comprising stem cells having a transgene encoding CXCR4 (e.g., Figure 3) which is a type of isolated cell population. It is known in the art that peripheral blood contains some hematopoietic stem cells. Therefore, the examiner concludes that Sawada anticipates an isolated population of stem cells having a transgene encoding CXCR4, wherein the isolated population comprises a high amount of immature primitive progenitor cells. The examiner points out that the specification does not provide a limiting definition for the phrase "a high amount of immature primitive progenitor cells."

Claim 18 is directed to the isolated population of stem cells according to claim 17, wherein the stem cells are hematopoietic stem cells. The transgenic mouse of Sawada et al. comprises a cell population comprising hematopoietic stem cells having the CXCR4 gene. Sawada et al. provide isolated peripheral blood from the transgenic mouse a transgene encoding CXCR4. Peripheral blood is known in the art to have some hematopoietic stem cells. Therefore, the examiner concludes that Sawada anticipates an isolated population of hematopoietic stem cells having a transgene encoding CXCR4.

Claim 19 is directed to the population of cells according to claim 17 or 18, being capable of differentiating towards the myeloid and erythroid lineages. Sawada et al. indicate that immature myeloid and erythroid lineage cells are produced in their

transgenic mice (page 1444, Fig.3). These cell types can be found in peripheral blood of the transgenic mice.

Claims 24-25 are directed to limitations which affect the concentration of SDF-1, which can be used to stimulate the claimed isolated stem cell population. These claims do not further limit the structure of the isolated stem cell population of claim 1; rather they describe a characteristic of the cells under certain manipulated conditions. Therefore, the teachings of Sawada et al. satisfy the limitations of claims 24-25.

Accordingly, Sawada et al. anticipated the instant claims.

Petit

The rejection of claims 17-25 under 35 U.S.C. 102(b) as being anticipated by Petit et al (Nature Immunology. July 2002; 3(7): 687-694, 787) is withdrawn in response to the applicant's claim amendments.

The applicant's claim amendments have been fully considered and are persuasive. The applicant has amended the claims to recite an "isolated population of stem cells comprising a transgene encoding CXCR4." Without a doubt, the population contains the transgene, CXCR4. Petit does not teach cells having the CXCR4 transgene. Accordingly, Petit does not anticipate the amended claims.

Therefore, the examiner hereby withdraws the rejection of claims 17-25 under 35 U.S.C. 102(b) as being anticipated by Petit et al.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 17-25 remain under 35 U.S.C. 103(a) as being unpatentable over Sawada et al (J. Exp. Med., May 4, 1998; 187(9): 1439-1449) in view of Lapidot et al. (Leukemia. October 2002; 16(1): 1992-2003) for the reasons of record and the comments below.

The applicant's arguments have been fully considered but are unpersuasive.

The applicant reiterates the argument provided under the anticipation rejection, that Sawada does not teach an isolated population of stem cells comprising a transgene encoding CXCR4, but merely a transgenic animal comprising the transgene CXCR4. As discussed above, the examiner interprets Sawada as possessing an isolated population of stem cells comprising a transgene encoding CXCR4. Sawada was in the possession of peripheral blood from a transgenic mouse comprising stem cells having a transgene encoding CXCR4 (e.g., Figure 3) which is a type of isolated cell population. It is known in the art that peripheral blood contains some hematopoietic stem cells. Therefore, the examiner concludes that Sawada anticipates an isolated population of stem cells having a transgene encoding CXCR4. Accordingly, the examiner finds this argument unpersuasive.

The applicant further argues that Lapidot does not cure the deficiencies of Sawada. The applicant further argues that Lapidot's general discussion of stem cell subpopulations cited by the Office would not motivate one of ordinary skill to modify the teachings of Sawada. The examiner indicated Sawada et al. does not explicitly teach the limitations of claims 21-23 wherein the isolated population of stem cells comprises $CD34^{+}/CD38^{-/low}$ progenitor cells. The examiner uses Lapidot to supplement the teachings of Sawada to show that $CD34^{+}/CD38^{-/low}$ progenitor cells are present in the peripheral blood of Sawada. Lapidot teach cord blood contains primitive $CD34^{+}/CD38^{-/low}$ stem cells which are up to 5% of total $CD34^{+}$ cells. (page 1994, col.2). Furthermore, Lapidot teaches that $CD34^{+}/CD38^{-/low}$ progenitor cells can be found in peripheral blood, thereby demonstrating that peripheral blood contains an isolated population of stem cells having $CD34^{+}/CD38^{-/low}$ progenitor cells. Therefore, the applicant's arguments are unpersuasive.

Therefore, the examiner hereby maintains the rejection of claims 17-25 under 35 U.S.C. 103(a) as being unpatentable over Sawada et al (J. Exp. Med., May 4, 1998; 187(9): 1439-1449) in view of Lapidot et al. (Leukemia. October 2002; 16(1): 1992-2003).

The examiner reiterates the pending rejection:

Claims 17-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawada et al (J. Exp. Med., May 4, 1998; 187(9): 1439-1449) in view of Lapidot et al. (Leukemia. October 2002; 16(1): 1992-2003).

Claim 17 is directed to an isolated population of stem cells comprising a transgene encoding CXCR4 and exhibiting improved CXCR4 signaling capability in response to low and/or high concentration of SDF-1, wherein the isolated population comprises a high amount of immature primitive progenitors. Sawada et al. teach a transgenic mouse comprising a human CXCR4 gene (page 1440, Materials). The transgenic mouse comprises a cell population comprising stem cells having the CXCR4 gene. Sawada was in the possession of peripheral blood from a transgenic mouse comprising stem cells having a transgene encoding CXCR4 (e.g., Figure 3) which is a type of isolated cell population. It is known in the art that peripheral blood contains some hematopoietic stem cells. Therefore, the examiner concludes that Sawada anticipates an isolated population of stem cells having a transgene encoding CXCR4, wherein the isolated population comprises a high amount of immature primitive progenitor cells. The examiner points out that the specification does not provide a limiting definition for the phrase "a high amount of immature primitive progenitor cells."

Claim 18 is directed to the isolated population of stem cells according to claim 17, wherein the stem cells are hematopoietic stem cells. The transgenic mouse of Sawada et al. comprises a cell population comprising hematopoietic stem cells having the CXCR4 gene. Sawada et al. provide isolated peripheral blood from the transgenic mouse a transgene encoding CXCR4. Peripheral blood is known in the art to have some hematopoietic stem cells. Therefore, the examiner concludes that Sawada anticipates an isolated population of hematopoietic stem cells having a transgene encoding CXCR4.

Claim 19 is directed to the population of cells according to claim 17 or 18, being capable of differentiating towards the myeloid and erythroid lineages. Sawada et al. indicate that immature myeloid and erythroid lineage cells are produced in their transgenic mice (page 1444, Fig.3). These cell types can be found in peripheral blood of the transgenic mice.

Claims 24-25 are directed to limitations which affect the concentration of SDF-1, which can be used to stimulate the claimed isolated stem cell population. These claims do not further limit the structure of the isolated stem cell population of claim 1; rather they describe a characteristic of the cells under certain manipulated conditions. Therefore, the teachings of Sawada et al. satisfy the limitations of claims 24-25.

Sawada et al. does not explicitly teach the limitations of claims 21-23 wherein the population of cells comprises $CD34^+/CD38^{-/low}$ progenitor cells.

However, Lapidot teach cord blood contains primitive $CD34^+/CD38^{-/low}$ stem cells which are up to 5% of total $CD34^+$ cells. (page 1994, col.2). Therefore, Lapidot et al. indicate that $CD34^+/CD38^{-/low}$ cells are immature primitive progenitor cells (claim 21), which are about 1-5% of the population (claim 22) and are at least about 3% of the population (claim 23). Since the scope of the population is not precisely defined by the claims or specification, the examiner concludes that Lapidot teaches the ranges recited in the instant claims. The examiner uses Lapidot to supplement the teachings of Sawada to show that $CD34^+/CD38^{-/low}$ progenitor cells are present in the peripheral blood of Sawada. Lapidot teach cord blood contains primitive $CD34^+/CD38^{-/low}$ stem cells which are up to 5% of total $CD34^+$ cells. (page 1994, col.2). Furthermore, Lapidot

teaches that $CD34^{+}/CD38^{-/low}$ progenitor cells can be found in peripheral blood, thereby demonstrating that peripheral blood contains an isolated population of stem cells having $CD34^{+}/CD38^{-/low}$ progenitor cells.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to combine the teachings of Sawada and Lapidot to deduce that the cell populations of Sawada et al. contain $CD34^{+}/CD38^{-/low}$ transgenic stem cells comprising CXCR4.

The person of ordinary skill in the art would have been motivated to make those modifications because Lapidot et al. describe the transgenic mice of Sawada et al. which overexpress human CXCR4 as having hematopoietic stem cells. Lapidot et al. teach that mammals have a population of immature primitive progenitor cells in cord blood and peripheral blood which are $CD34^{+}/CD38^{-/low}$ cells which are about 1-5% of the population. While not stating that the animals of Sawada et al. have $CD34^{+}/CD38^{-/low}$ cells which are transgenic for CXCR4 and which are about 1-5% of the population, there is strong suggestion that overexpressing CXCR4 has not altered the percentage of $CD34^{+}/CD38^{-/low}$ cells in the cord blood or peripheral blood population of the transgenic mice.

The skilled artisan would have had a reasonable expectation of success in combining the teachings of Sawada et al. and Lapidot et al. because each of these teachings describe populations of cells from the Sawada transgenic mice.

Therefore the isolated population of stem cells as taught by Sawada et al. in view of Lapidot et al. would have been *prima facie* obvious over the isolated population of stem cells of the instant application.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Scott Long/
Patent Examiner, Art Unit 1633